

Critical and Subcritical Ischaemia

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Objectives: To stratify leg ischaemia into high and low risk groups with respect to outcome.

Methods: An evaluation of 20 recent publications, reporting the results of 6118 patients with critical ischaemia. Low and high risk patient groups are identified by the definition of critical ischaemia. These groups are analysed with respect to outcome of the patient and limb.

Main outcome measures: Major amputation and mortality.

Results: From these data subcritical (rest pain and/or ankle pressure >40 mmHg, n=4089) and critical (tissue loss and/or ankle pressure <40 mmHg, n=2029) risk group of patients was identified. The 1, 3 and 5-year mortality is 26%, 44% and 56% with or without reconstruction. For patients in the low risk group, 27% did not lose their leg within the year if treated conservatively. For patients in the high risk group, amputation was required by 95% if treated conservatively, compared to 25% if treated with arterial reconstruction.

Conclusion: Reconstructive surgery should be viewed from the following, more realistic, perspective. For patients with rest pain (and/or ankle pressure >40 mmHg), 100% cumulative patency is equivalent to 64% resolution of symptoms at 1 year, as the rest may have improved without treatment. For high risk patients (tissue loss and/or ankle pressure <40 mmHg), 100% cumulative patency is equivalent to 93% limb salvage at 1 year. Future reports should identify these two groups separately, as the dominant difference between outcome studies is the proportion of subcritical patients in the study rather than better surgical or radiological techniques. This stratification also has an important bearing on pharmacotherapy trials.

Introduction

There are enormous discrepancies between the reported results of arterial reconstruction from different centres. Much of this is due to the inappropriate inclusion of patients with non-critical limbs into studies on chronic critical leg ischaemia.¹ Several definitions of critical ischaemia have recently been produced, all of which fail to predict eventual outcome with any degree of precision.² Nevertheless, the definitions imply that the outcome depends on the degree of ischaemia.

The natural history of these patients is extremely difficult to study, as most undergo some type of interventional procedure. Nevertheless, it is apparent that in most publications reporting the results of critical ischaemia there are two distinct groups with respect to outcome. There is a lower risk group consisting of patients with rest pain, not always with a low ankle pressure (hereafter called subcritical ischaemia). In addition, there is a higher risk group consisting of

those patients with true limb-threatening disease, i.e. those with tissue loss and/or ankle pressure <40 mmHg (hereafter called critical ischaemia (Table 1).

The aim of this study is to use the definition of critical ischaemia (Table 2) and apply it to patients obtained from a review of recent publications in order to determine the effect of treatment on these patients according to the severity of their ischaemia.

Methods

Twenty recent publications^{1,3-21} containing details of 6118 patients with "critical ischaemia" have been reviewed (Table 3). All patients have either been treated

Table 1. Critical ischaemic groups with respect to outcome.

Group	Inclusion criteria	
1. Lower risk (subcritical ischaemia)	Rest pain	and ankle pressure >40 mmHg
2. High risk (critical ischaemia)	Rest pain	Tissue loss and/or ankle pressure <40 mmHg

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Table 2. Definitions of critical ischaemia.

1. <i>Fontaine Classification</i> ²⁶	
Stage 3	Rest pain caused by arterial disease
Stage 4	Ulceration and/or gangrene caused by arterial disease
2. <i>International Vascular Symposium Working Party Definition</i> ²⁴	
1.	Severe rest pain requiring opiate analgesia for at least 4 weeks and either:
2.	Ankle pressure <40 mmHg or:
3.	Ankle pressure <60 mmHg in the presence of tissue necrosis or digital gangrene (Diabetics should be excluded from the ideal clinical study)
3. <i>Modified International Vascular Symposium Working Party Definition</i> ²	
1.	Severe rest pain requiring opiate analgesia for at least 4 weeks and either:
2.	Ankle pressure <40 mmHg or:
3.	Tissue necrosis or digital gangrene
4. <i>First European Working Group Definition</i> ²⁵	
1.	Severe rest pain requiring opiate analgesia for at least 2 weeks or:
2.	Ulceration or gangrene and:
3.	Ankle pressure <50 mmHg
5. <i>Second European Consensus Document</i> ²³	
1.	Persistently recurring ischaemic rest pain requiring analgesia >2 weeks and: Ankle systolic pressure <50 mmHg and/or: Toe systolic pressure <30 mmHg or:
2.	Ulceration or gangrene of the foot or toes and: Ankle systolic pressure <50 mmHg or: Toe systolic pressure <30 mmHg

Table 3. Twenty recent critical ischaemia publications (n = 6118).

Author	Year	No. patients
Finch ³	1980	145
Crawford ⁴	1981	230
Rush ⁵	1981	256
Towne ⁶	1981	154
Veith ⁷	1981	679
Mosley ⁹	1986	66
Jamieson ⁸	1983	64
Wolfe ¹⁰	1988	428
Beard ¹¹	1989	79
Taylor ¹²	1990	387
Dormandy ¹³	1990	Review
Taylor ¹⁴	1991	498
da Silva ¹⁵	1993	679
Thompson ¹	1993	148
Paaske ¹⁶	1994	153
Aune ¹⁷	1994	271
Troeng ¹⁸	1994	690
Schroeder ¹⁹	1994	1065
Currie ²⁰	1994	50
Wyatt ²¹	1994	76

conservatively, received reconstructive surgery or angioplasty, or had an amputation. All treatment types are considered in the analysis.

Each paper utilises at least one of the existing definitions of critical ischaemia (Table 2). These criteria are noted when analysing each report, and patients defined as either low or high risk dependent upon the presence of rest pain or tissue loss or an ankle pressure of above or below 40 mmHg respectively (Table 1). These low and high risk groups are further analysed with respect to patient survival and limb salvage. True life-table analysis requires absolute numbers, and these are not presented in most publications. The calculations in this study are not complex, and each study has merely been weighted for patient number at each time point prior to inclusion in patient survival and limb salvage calculations.

For each group we then predicted the outcome of critical ischaemia with respect to mortality. In addition, the relative benefits of conservative therapy with respect to resolution of symptoms, and reconstructive surgery with respect to limb salvage, can be assessed.

Results

Data analysis from these 20 studies^{1,3-21} reveals a low risk group of 4089 patients with rest pain and/or a high ankle pressure (>40 mmHg), subcritical ischaemia, and a high risk group of 2029 patients who have either tissue loss and/or a recorded ankle pressure of less than 40 mmHg (approximate ratio low:high risk = 2:1) critical ischaemia.

Outcome for all 6118 patients included in this study is shown in Fig. 1. The 1, 3 and 5-year mortality for all patients with critical ischaemia is 26%, 44% and 56%, respectively. This compares with a 1, 3 and 5-year mortality of 5%, 10% and 25% in an age and sex matched control group of patients without vascular disease.²²

At 1 year, 73% of patients in the low risk group lost their leg or died if treated conservatively (Fig. 1). For those patients fitting the high risk criteria, 95% of those treated conservatively required amputation within a year. By comparison, for those high risk patients who received reconstruction, only 25% required major amputation.

From these data, comment can be made on the effect of treatment on the natural history of critical ischaemia (Fig. 2). For patients in the high risk group, 26% will be dead whatever the mode of treatment and 5% will not be amputated if treated conservatively. This leaves 69% alive and potentially improved by intervention at 1 year.

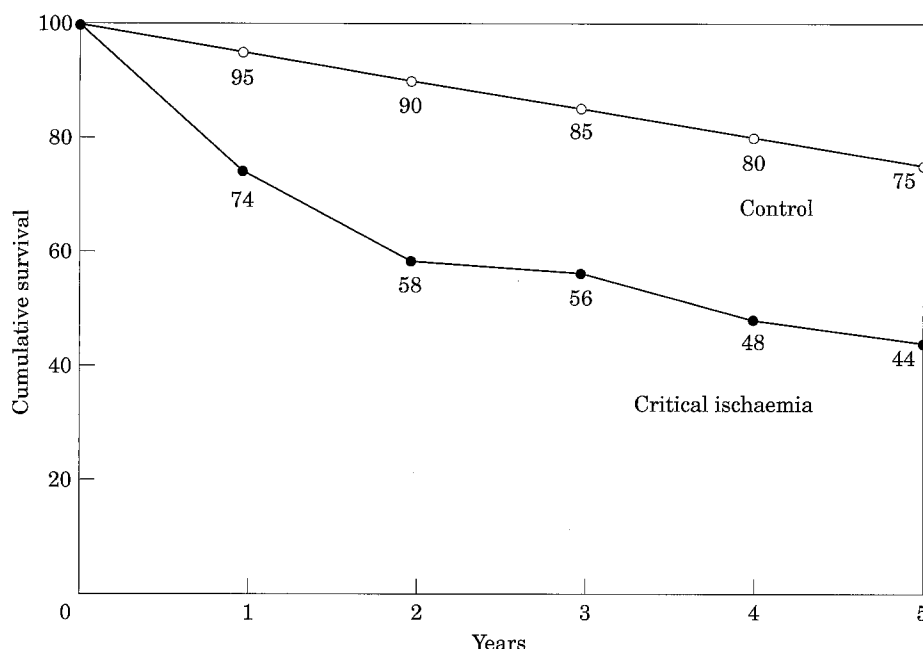


Fig. 1. Survival of patients with critical ischaemia ($n=6118$) compared with an age and sex matched control.⁽²³⁾

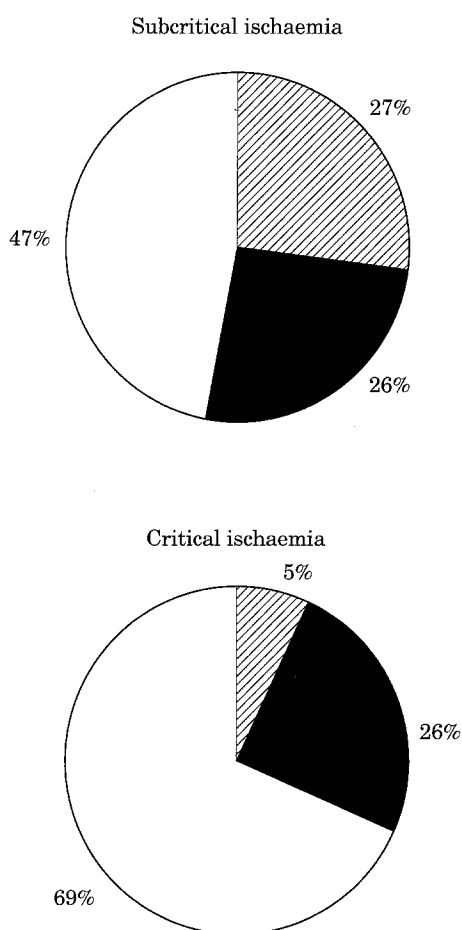


Fig. 2. Pie charts showing outcome of low and high risk critical ischaemia patients at 1 year (% patients).

Mortality data concerning the low risk group is less secure due to our inability to obtain a separate 1 year mortality for this patient group. Again, 26% of patients are dead at 1 year despite treatment. Added to the 27% whose symptoms would have improved with conservative treatment, this leaves 47% potentially improved by intervention.

Discussion

The major purpose of defining and grading ischaemia is to clarify the reports and allow reasonable comparison between different studies. Many of the gross differences in reported results are due to the inclusion of a variable proportion of patients with a grim outlook. "Limb salvage" includes an ill-defined melange of patients, hence the need for "critical ischaemia". This definition, with all its flaws, has been abused: it is impossible for all patients to have either claudication or critical ischaemia, since some will have rest pain and not meet the definition, yet surgical journals are littered with such reports. We therefore set out to identify a "low risk group" and a "high risk group" of patients with rest pain \pm tissue loss.

High risk patients had rest pain and either tissue loss or an ankle pressure <40 mmHg (critical ischaemia). Low risk patients had rest pain, an intact foot and an ankle pressure >40 mmHg (subcritical ischaemia).

Data from the Joint Vascular Research Group Study

from 16 centres in the United Kingdom summarised the outcome of critical leg ischaemia as follows: at 1 year 20% of patients died, 25% of patients lost one leg and only 55% were alive with both legs.¹⁰ The present analysis confirms these findings and in addition identifies a high risk patient group, in whom only 5% survived with an intact limb unless they had successful surgical intervention. This supports our prejudice and makes it very difficult to perform randomised studies to try and predict a group of critically ischaemic limbs which might benefit from a less invasive approach.

It was previously assumed that all patients with severe ischaemia would at some stage require a major amputation if not treated surgically. Although data concerning the natural history for the conservative treatment of critical ischaemia is sparse,²³ we do know that a proportion of these limbs do not progress to amputation. In some instances conservative or medical treatment of patients with leg ischaemia may be sufficient.

Unfortunately, to date no definition of critical ischaemia provides good enough specificity and sensitivity to predict those patients who are at lower risk of amputation.² The Fontaine classification²⁶ has been more useful than "limb salvage" and subcritical and critical ischaemia are similar to Fontaine III and Fontaine IV. There are, however, important differences; it has been shown that in a large cohort of patients the outcome of rest pain and an ankle pressure <40 mmHg (Fontaine III) is similar to rest pain with tissue loss (Fontaine IV).² Critical ischaemia therefore includes patients in the most severe category, who would be excluded from Fontaine IV.

In a recent retrospective study of 136 critically ischaemic limbs treated conservatively, the 1-year limb salvage rate was 54%.²⁷ At the same time interval, patient survival was 46% and only 25% of all patients were alive with both legs. In other words, even if these patients had been suitable for intervention, the 1-year outcome would only have been improved in 75% of patients. Although the current European definition of critical ischaemia was used in that study, no higher risk group was identified. Indeed, all the current definitions of critical ischaemia have been criticised for not being able to predict outcome accurately.¹

The results of the present analysis go some way towards predicting the natural history of patients receiving conservative therapy for the treatment of critical ischaemia. By applying the criteria of rest pain or tissue loss and/or an ankle pressure of above or below 40 mmHg applied retrospectively to several recent publications on critical ischaemia, it appears that this patient group can be sub-divided into low and high

risk groups with respect to outcome. Comment can then be made on the natural history of patients with critical ischaemia who do not receive revascularisation procedures. For those in the lower risk group, the 1-year actual limb salvage of 27% is considerably better than that of 5% for the higher risk group.

For surviving patients in the lower risk group, 100% cumulative patency is equivalent to only 64% resolution of symptoms at 1 year (i.e. 36% of surviving patients would have benefited from conservative treatment, Fig. 2).

The limb outcome following intervention is different for patients in the high risk group. Here, 100% cumulative patency is equivalent to 93% limb salvage at 1 year (ie 93% of survivors have benefited from surgery at 1 year). For this group, intervention is usually essential for limb viability to be maintained. There is no evidence that the use of pharmacotherapy, sympathectomy or spinal cord stimulation can improve limb salvage for these patients. There are, therefore, a group of patients with critical ischaemia (tissue loss \pm an ankle pressure of <40 mmHg) in whom surgical/radiological intervention appears to be virtually imperative to save the limb. There is a less severely affected group for whom we suggest the term subcritical ischaemia (tissues intact and an ankle pressure of >40 mmHg) in whom limb loss does not appear to be inevitable and pharmacotherapy and medical treatment may buy sufficient time for the crisis to pass. Pharmacotherapy trials confined to patients in this second group are likely to be more valid, as limbs unsalvageable by drugs alone have been removed from the study.

In conclusion, we would suggest separation into "subcritical" and "critical" when studying patients with leg ischaemia. Only by appreciating the different natural histories of rest pain and tissue loss can we assess accurately the beneficial results of revascularisation procedures for critical ischaemia. We recommend that future reports should measure results against the predicted outcomes, if the true effects of intervention are to be fully appreciated.

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